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Original Article - Supplementary file

Effectiveness and Safety of Originator and Biosimilar G-CSF as Primary Prophylaxis in DLBCL: A Cohort Study and Meta-Analysis

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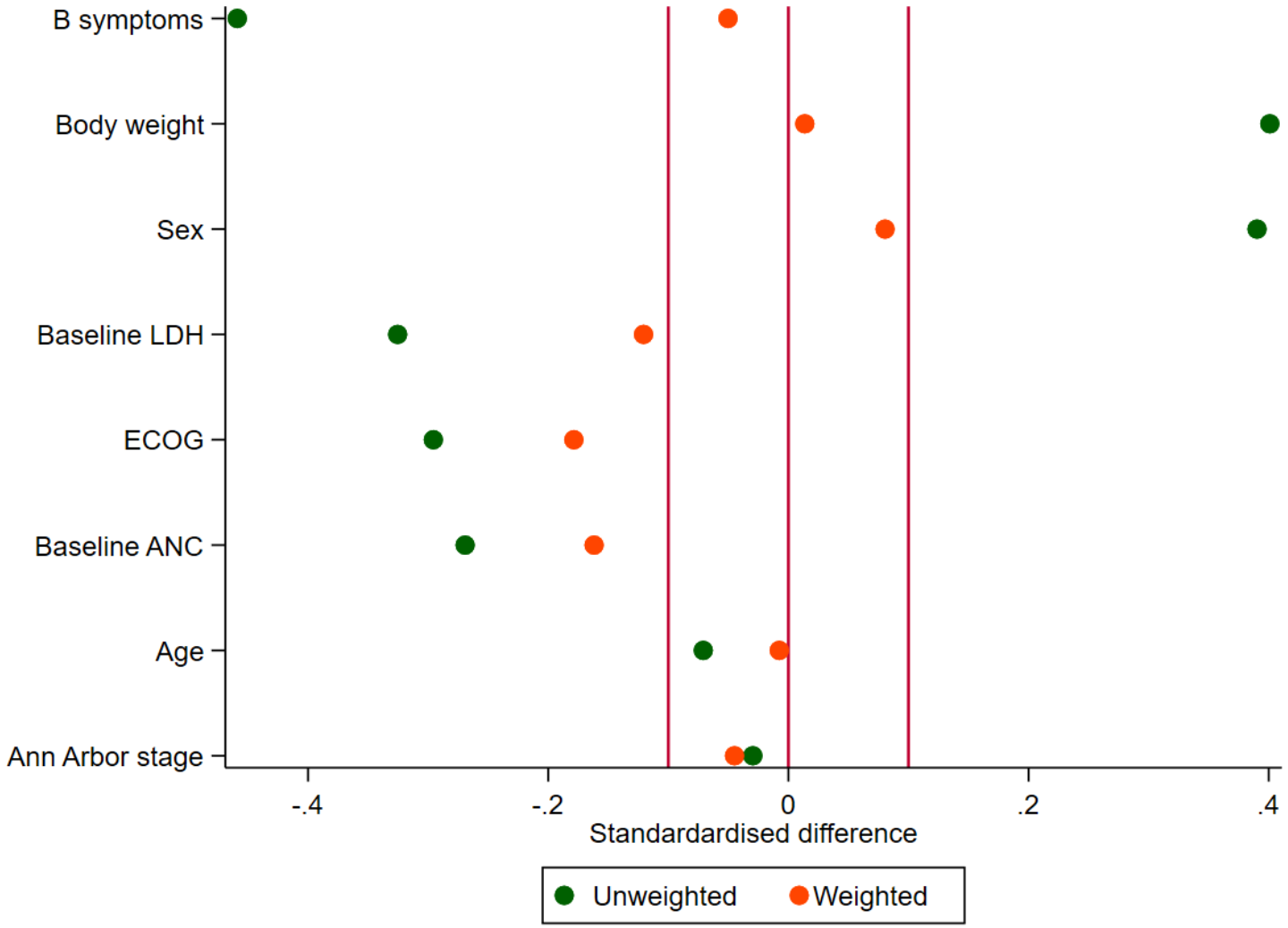
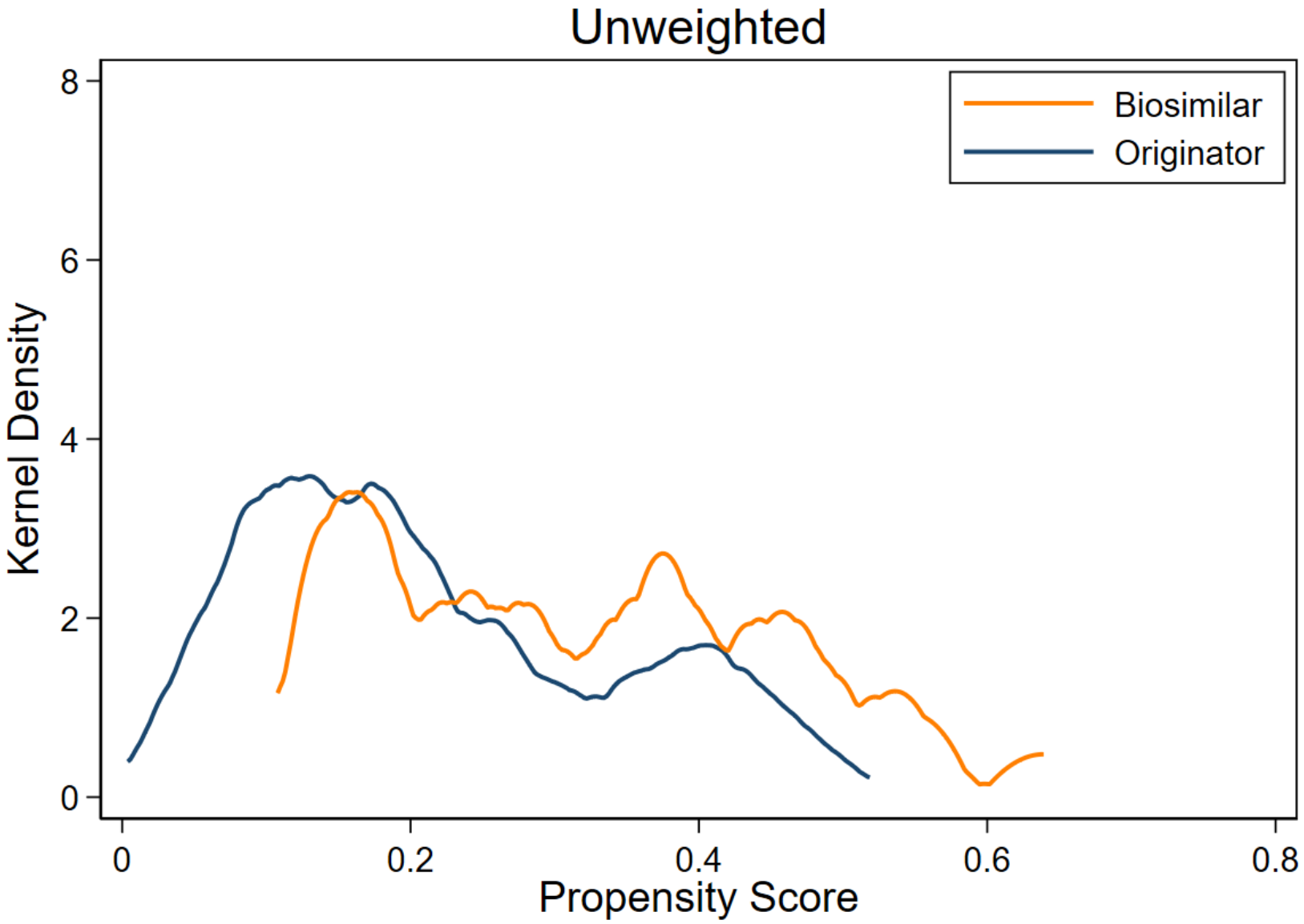
Supplementary Fig. 1. The standardised mean differences of each independent variable before and after IPTW adjustment

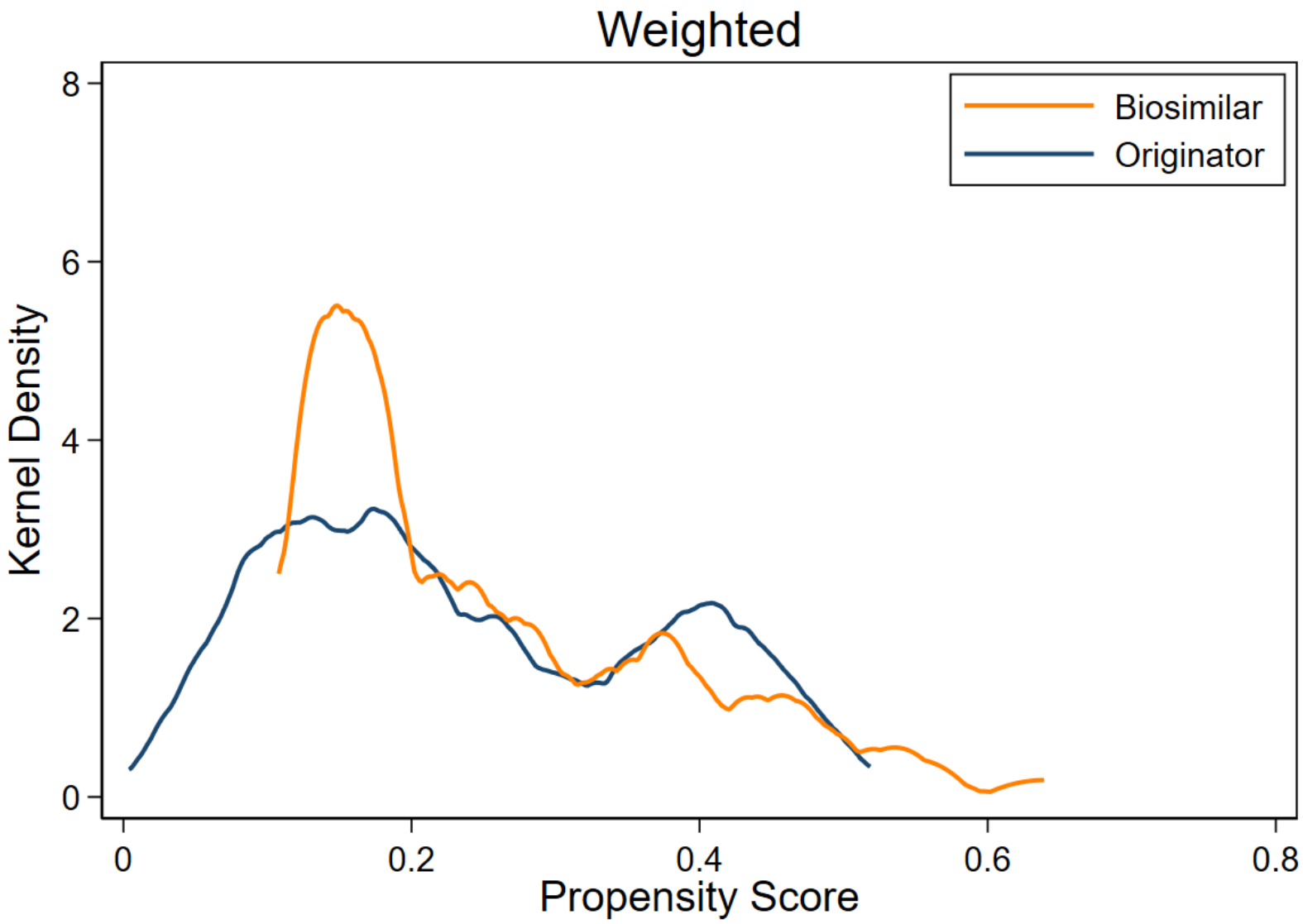


Abbreviation: IPTW, inverse probability of treatment weighting

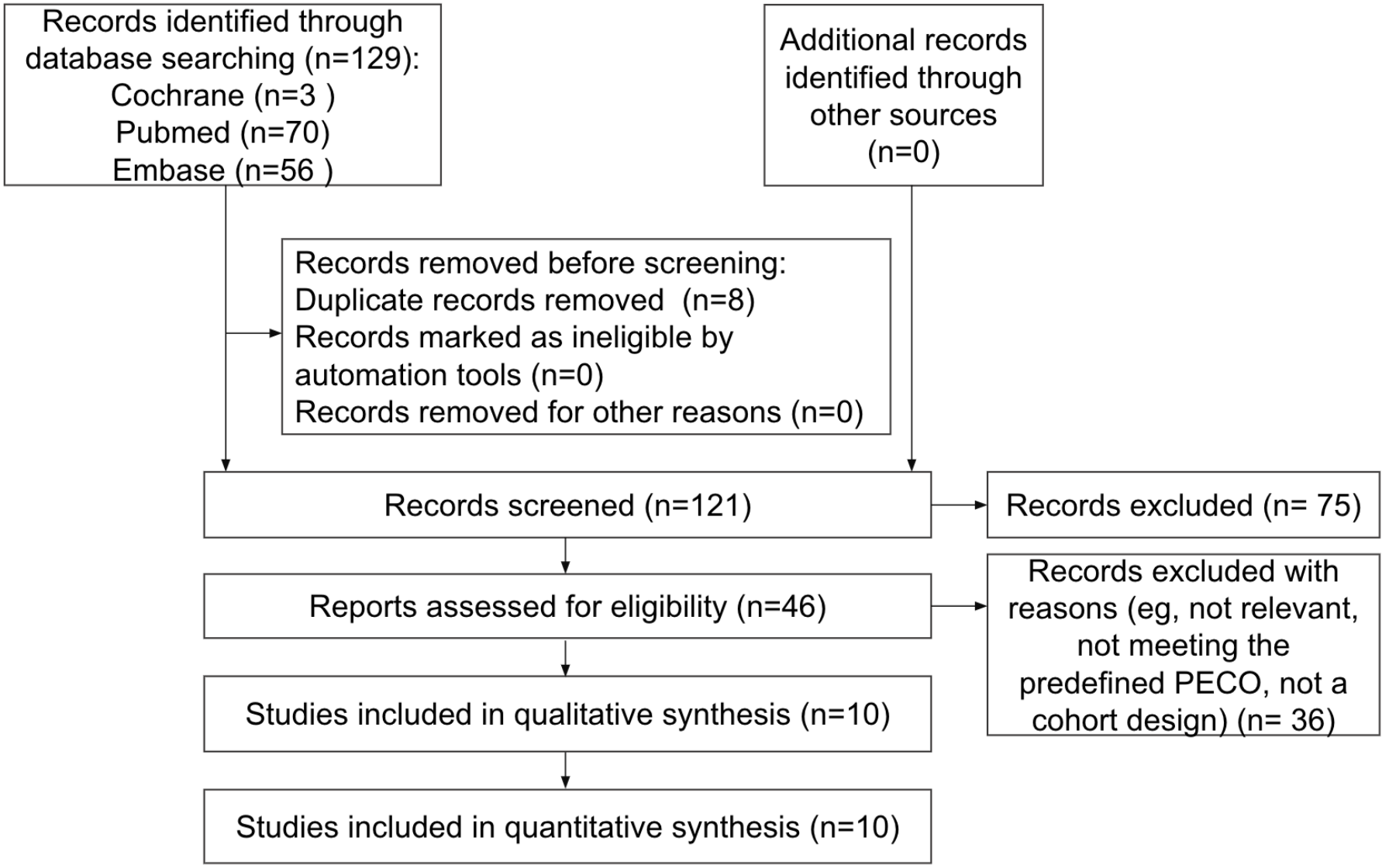
Supplementary Fig. 2a. The distribution of propensity scores in the unweighted cohort



Supplementary Fig. 2b. The distribution of propensity scores in the weighted cohort

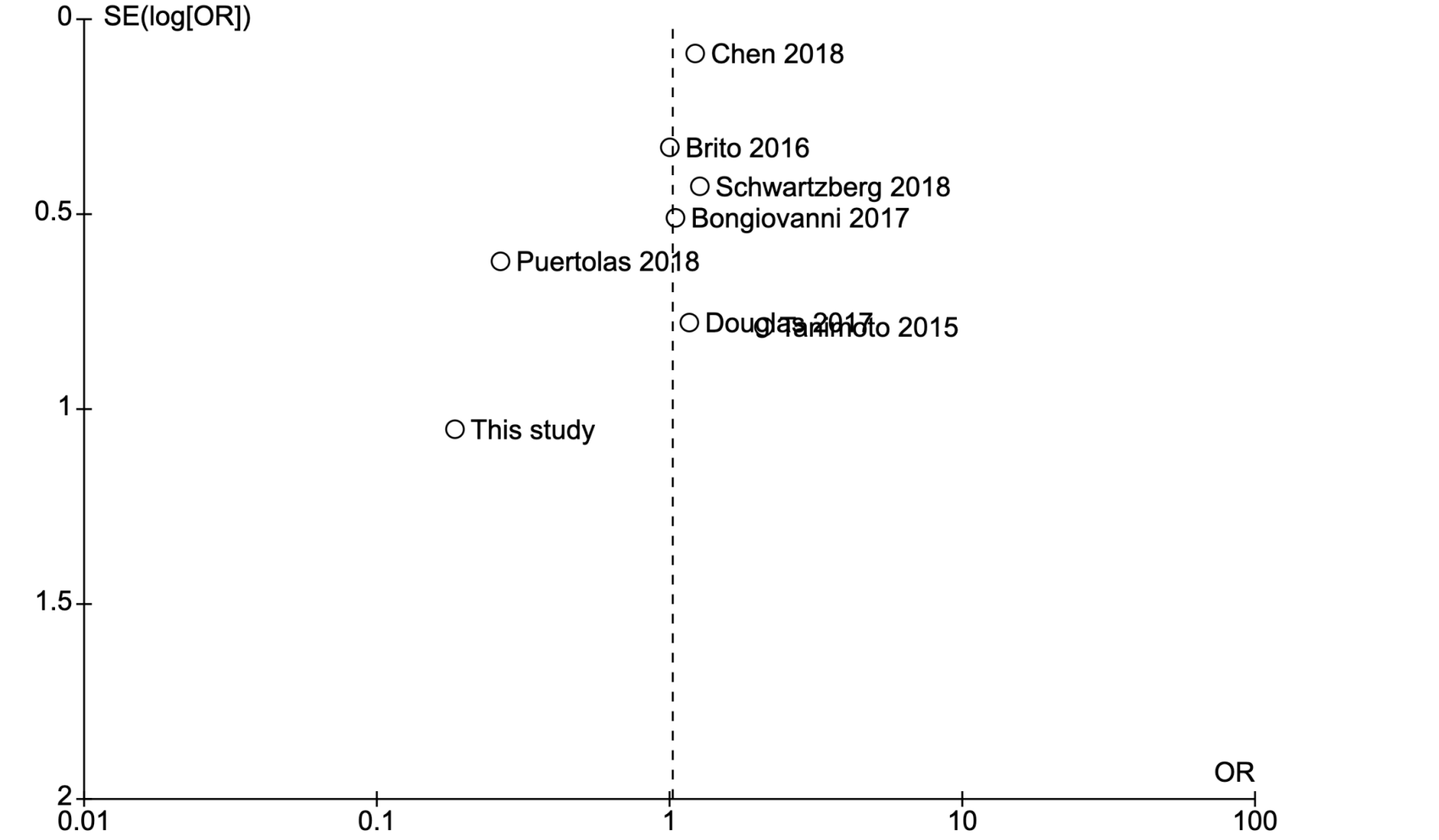


Supplementary Fig. 3. PRISMA diagram for study selection



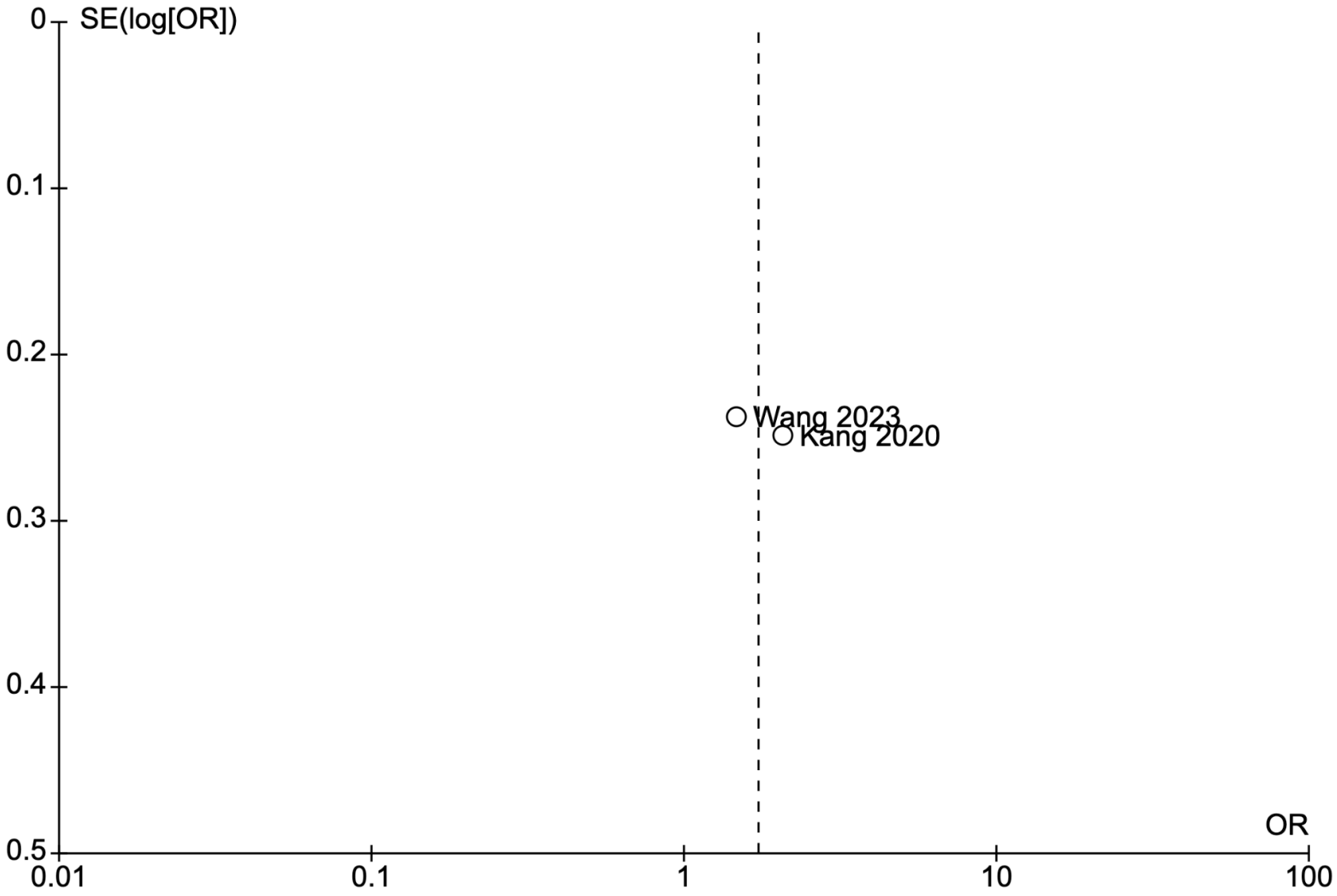
Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Supplementary Fig. 4a. Funnel plot for short-acting G-CSF



Abbreviation: G-CSF, granulocyte colony-stimulating factor

Supplementary Fig. 4b. Funnel plot for long-acting G-CSF



Abbreviation: G-CSF, granulocyte colony-stimulating factor

Supplementary Table 1. Characteristics of the included studies

Author	Country	Design	Data source	G-CSF type	Cancer type	Sample size	Definition of outcome	Follow-up period
This study	Taiwan	Retrospective, single-center	EHR	Short-acting and long-acing	DLBCL	Ori: 105 BS: 29	A temperature of >38.3°C or > 38.0°C sustained for 1 hour, and ANC < 500/μL or ANC < 1000/μL but predicted to decline to ≤ 500/μL over the next 48 hours	The entire duration of chemotherapy (at least 1 cycle)
Chen 2018 [13]	USA	Retrospective, nationwide	Administrative health claims data	Short-acting	Unrestricted	Ori: 9671 BS: 1531	Neutropenia or fever requiring hospitalizations	21 days after the earliest filgrastim use
Douglas 2017 [23]	USA	Retrospective, nationwide	Administrative claims from the Humana Research Database	Short-acting	Unrestricted	Ori: 88 BS: 101	1. Broad definition: diagnosis of infection and/or neutropenia 2. Narrow definition: infection and neutropenia diagnoses	At least 6 days of continuous plan enrollment before the index date [i.e., date of the first claim for a filgrastim product] to verify chemotherapy exposure and 14 days of continuous enrollment after the index date
Tanimoto 2015 [24]	Japan	Retrospective, multicenter	EHR	Short-acting	Non-Hodgkin lymphoma	Ori: 26 BS: 12	Not explicitly stated	At least two cycles of CHOP or R-CHOP
Puértolas 2018 [25]	Spain	Retrospective, multicenter	EHR	Short-acting	Breast cancer	Ori: 35 BS: 303	Febrile neutropenia (A single temperature of 38.3 °C or a sustained temperature of ≥ 38 °C for more than 1 hour and ANC < 1000 cells/mm^3)	The entire duration of chemotherapy (at least 1 cycle)
Schwartzberg 2018 [26]	USA	Retrospective, nationwide	Optum Research Database	Short-acting	Non-myeloid cancer	Ori: 3297 BS: 162	A combination of diagnosis codes for neutropenia, fever, or bacterial or fungal infection	Follow-up commenced after the last dose of filgrastim in the first observed

								chemotherapy cycle or the fifth day after the index date (first G-CSF use), whichever was earlier to the end of the cycle
Bongiovanni 2017 [27]	Italy	Retrospective, single-center	EHR	Short-acting	Soft tissue sarcomas	Ori: 42 BS: 25	Febrile neutropenia (<1000/mm^3 ANC and a single temperature of >38.3 °C or a sustained temperature of ≥38 °C for more than 1 hour)	59 months (overall survival in relation to the type of G-CSF use was also assessed)
Brito 2016 [28]	Portugal	Retrospective, single-center	EHR	Short-acting	Breast cancer	Ori: 147 BS: 134	Febrile neutropenia (Temperature ≥ 38 °C concurrent with ANC ≤ 500 cells/μL)	The entire duration of chemotherapy (at least 1 cycle)
Wang 2023 [29]	USA	Retrospective, nationwide	2019 IBM MarketScan databases	Long-acting	Breast, lung, colorectal, esophageal and gastric, pancreatic, prostate, ovarian, non-Hodgkin lymphomas	Ori: 633[a] BS: 633[a]	1. Broad definition: neutropenia, fever, or infection diagnosis code in any position 2. Narrow definition: neutropenia diagnosis code in any position	A minimum of 1 month of follow-up; if data are available, up to 8 consecutive qualifying cycles
Kang 2020 [30]	South Korea	Retrospective, single-center	EHR	Long-acting	DLBCL	Ori: 193 BS: 103	A temperature of >38.3°C or > 38.0°C sustained for 1 hour, and ANC < 500/μL or ANC < 1000/μL but predicted to decline to ≤ 500/μL over the next 48 hours	The entire duration of chemotherapy (at least 1 cycle)

Abbreviation: ANC, absolute neutrophil count; BS, biosimilar; CHOP, cyclophosphamide/doxorubicin/vincristine/prednisolone; DLBCL, diffuse large b cell lymphoma; EHR, electronic health record; G-CSF, granulocyte colony-stimulating factor; Ori, originator; R-CHOP,

rituximab/cyclophosphamide/doxorubicin/vincristine/prednisolone; USA, United States of America

[a] One of two propensity score-matched analyses

Supplementary Table 2. Risk of bias assessment by Newcastle–Ottawa scale (NOS)

Item		This study	Chen 2018 [13]	Douglas 2017 [23]	Tanimoto 2015 [24]	Puértolas 2018 [25]	Schwartz-berg 2018 [26]	Bongiova-nni 2017 [27]	Brito 2016 [28]	Wang 2023 [29]	Kang 2020 [30]
Selection	Representative-ness of the exposed cohort	*	*	*	*	*	*	*	*	*	*
	Selection of the non exposed cohort	*	*	*	*	*	*	*	*	*	*
	Ascertainment of exposure	*	*	*	*	*	*	*	*	*	*
	Demonstration that outcome of interest was not present at start of study	*	*	*	*	*	*	*	*	*	*
Compara-bility	Comparability of cohorts on the basis of the design or analysis	**	**	*	0	*	**	*	*	*	*
Outcome	Assessment of outcome	*	*	*	*	*	*	*	*	*	*
	Was follow-up long enough for outcomes to occur	*	*	*	*	*	*	*	*	*	*
	Adequacy of	*	*	*	*	*	*	*	*	*	*

	follow up of cohorts										
NOS quality scores		9	9	8	7	8	9	8	8	8	8